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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/026,459	02/19/1998	HONG-JI XU	UTXC:506	1781

7590

01/30/2003

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EXAMINER

SHUKLA, RAM R

ART UNIT

PAPER NUMBER

1632

DATE MAILED: 01/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/026,459

Applicant(s)

XU ET AL.

Examiner

Ram R. Shukla

Art Unit

1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 October 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,11,12,21-30,36,37 and 49-61 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

- 5) ☒ Claim(s) 1,11,12 and 49-60 is/are allowed.

- 6) ☐ Claim(s) 21-30,36,37 and 61 is/are rejected.

- 7) ☐ Claim(s) _____ is/are objected to.

- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on _____ is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 26.

- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10-10-02 has been entered.
2. The amendment filed 10-10-02 has been entered.
3. Claims 2-10, 13, 14, 16-20, 31-34 and 44-48 have been cancelled.
4. Amendments to claims 1, 11, 12, 21, 21-27 and 36 have been entered.
5. New claims 52-64 have been entered. Regarding the newly presented claims, it is noted that the numbering of claims is not accordance with 37 CFR 1.126, which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).
Misnumbered claims 52-64 have been renumbered as claims 49-61
- 6.
7. Claims 1, 11, 12, 21-30, 36, 37 and 49-61 are pending and under consideration.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.
8. Claims 27-30 and 36-37 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated host cell comprising

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the DNA of claims 1, 21 and 22 *in vitro*, does not reasonably provide enablement wherein the cell is present *in vivo*. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

It is noted that the claims as instantly present encompass host cells *in vitro* as well as *in vivo*. However, the invention is not enabling for a host cell *in vivo* because the specification as filed does not provide sufficient guidance as to how an artisan of skill would have delivered the DNA construct to a cell *in vivo* and an artisan of skill would have required undue experimentation to practice the claim commensurate with the full scope of the claims because the state of the art of delivering DNA to a cell *in vivo* was unpredictable and had several problems at the time of the invention and neither the specification nor the art of record teaches how to address these issues.

It is emphasized that while progress has been made in recent years for *in vivo* gene transfer, vector targeting *in vivo* to desired organs continues to be unpredictable and inefficient. This is supported by numerous teachings available in the art. For example, Deonarain (1998) discussed that one of the biggest problems hampering successful gene therapy is the "ability to target a gene to a significant population of cells and express it at adequate levels for a long enough period of time" (page 53, first paragraph). Deonarain reviews new techniques under experimentation in the art, which show promise, but is currently even less efficient than viral gene delivery (see page 65, first paragraph under Conclusion section). Verma et al. (1997) reviews various vectors known in the art for use in gene therapy and the problems which are associated with each and clearly indicated that at the time of the claimed invention resolution to vector targeting had not been achieved in the art (see entire article). Verma discusses the role of the immune system in inhibiting the efficient targeting of viral vectors such that efficient expression is not achieved (see page 239 and 2nd and 3rd column of page 242. Verma also indicates that appropriate enhancer-promoter sequences can improve expression, but that the "search for such [useful] combinations is a case of trial and error for a given cell type" (page 240, sentence bridging columns 2 and 3). Crystal also

reviews various vectors known in the art and indicates that "among the design hurdles for all vectors are the need to increase the efficiency of gene transfer, to increase target specificity and to enable the transferred gene to be regulated" (page 409). The specification fails to teach any specific targeting techniques, fails to provide any working examples, which encompass vector targeting, and fails to direct the skilled artisan to any teachings of targeting strategies known in the art, which would allow one of skill in the art to practice the claimed invention without undue experimentation.

In conclusion, the specification is not enabling for the claimed invention commensurate with the full scope of the claims and therefore limiting the scope of the claimed invention to an isolated host cell comprising the DNA of claims 1, 21 and 22 in vitro is proper.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

10. Claims 21 is rejected under 35 U.S.C. 102(e) as being anticipated by Shepard et al (US Patent 5710255, 1-20-1998).

The nucleic acid of SEQ ID NO 2 of Shepard et al will encode the protein of SEQ ID NO 37 (sequence comparison results). Accordingly, the nucleic acid of claims 21 is anticipated by Shepard et al.

11. Claims 21-30, 36, 37 and 61 are rejected under 35 U.S.C. 102(b) as being anticipated by Xu et al (US Patent 5,496,731, 3-5-1996).

The nt 124-3230 of the nucleic acid of SEQ ID NO 1 of Xu et al has 100% sequence identity with nt 7-3113 of SEQ ID NO 36 (see the sequence comparison). This art also teaches vectors, host cells, and nucleic acid compositions (see examples in columns 21-32). Accordingly, the nucleic acids of claims 21-30, 36, 37 and 64 are anticipated by Xu et al.

12. Claims 21-30, 36, 37 and 61 are rejected under 35 U.S.C. 102(b) as being anticipated by Lee et al (WO 90/05180, 1-17-1990).

The nucleic acid of Lee et al will encode the protein of SEQ ID NO 37 (sequence comparison results). This art also teaches vectors, host cells, and nucleic acid compositions (see pages 52-70). Accordingly, the invention of claims 21-30, 36, 37 and 56 is anticipated by Lee et al.

13. The 103 rejections of claims 1, 21-27 and 36 has been withdrawn in view of the applicants amendment of 10-10-02.

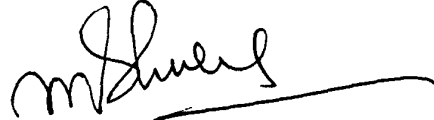
14. Claims 1, 11, 12, 49-60 are free of the prior art of record and are allowable.

When amending claims, applicants are advised to submit a clean version of each amended claim (without underlining and bracketing) according to § 1.121(c). For instructions, Applicants are referred to <http://www.uspto.gov/web/offices/dcom/olia/aipa/index.htm>.

Applicants are also requested to submit a copy of all the pending/under consideration claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ram R. Shukla whose telephone number is (703) 305-1677. The examiner can normally be reached on Monday through Friday from 7:30 am to 4:00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051. The fax phone number for this Group is (703) 308-4242. Any inquiry of a general nature, formal matters or relating to the status of this application or proceeding should be directed to the William Phillips whose telephone number is (703) 305-3413.

Ram R. Shukla, Ph.D.
Primary Examiner
Art Unit 1632


RAM R. SHUKLA, PH.D
PATENT EXAMINER